

Appl. No.: 10/578,962
Amdt. Dated December 8, 2010
Reply to Office Action of June 8, 2010

REMARKS/ARGUMENTS

Request for Continued Examination

Applicants file concurrently herewith a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114. The instant paper is Applicants required submission under 37 C.F.R. § 1.114 to accompany the RCE.

Status of the Claims

Claims 1-43, 46-55, and 57 are pending. Claims 36-38 are under examination and stand rejected. Claims 1-35, 39-43, 46-55, and 57 are withdrawn for being drawn to non-elected inventions.

Reexamination and reconsideration of the application are respectfully requested in view of the following remarks.

The Rejection of the Claims Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 36-38 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Klimyuk *et al.* (U.S. Patent Pub. No. 2004/0255347) in view of Rose ((2002) *RNA* 8:1444-1453) and GenBank Accession No. Z29370. This rejection is respectfully traversed.

The Office Action alleges that, given the recognition of those of ordinary skill in the art of expressing a gene of interest as taught by Klimyuk *et al.*, it would have been obvious to a person having ordinary skill in the art to generate an expression vector of Klimyuk *et al.* by inserting the intron of Rose into AT rich region of CrTMV RNA dependent RNA polymerase of Klimyuk *et al.* in view of GenBank Accession No. Z29370 resulting in Applicants' invention. The Office Action further alleges that one skilled in the art would have been motivated to do so given the teaching of Rose that insertion of a plant intron would enhance the expression or a

Appl. No.: 10/578,962
Amdt. Dated December 8, 2010
Reply to Office Action of June 8, 2010

gene of interest and the teaching of Klimyuk *et al.* that the expression system using viral RNA polymerase is limited by the low ability of RNA polymerase to provide function in trans.

Applicants respectfully disagree with this position of the Examiner and do not believe that the Examiner has stated a *prima facie* case of obviousness because the Examiner has ignored features of the claimed invention in stating his reasons for rejecting claims 36-38 as being as being unpatentable over Klimyuk *et al.* in view of Rose and GenBank Accession No. Z29370.

On page 4 of the Office Action, the Examiner states that Klimyuk *et al.* do not teach the limitation that one or more intron is inserted near or within A/U-rich localities of said sequence for replicon function whereby A/U rich localities are sequence stretches of at least 20 nucleotides in length with at least 55% NU-content or stretches of 6-9 nucleotides in a row of purely A/U containing sequence. Neither Rose nor GenBank Accession No. Z29370 teach the missing features. Regarding Rose, the Examiner does not even allege this. GenBank Accession No. Z29370 contains the genomic RNA of the RNA-dependent RNA polymerase and two other proteins from tobacco mosaic virus. However, GenBank Accession No. Z29370 is silent on introducing introns into A/U rich localities as recited in claim 36. The possibility that there are sequence stretches in GenBank Accession No. Z29370 of at least 20 nucleotides in length with at least 55% A/U-content or stretches of 6-9 nucleotides in a row of purely A/U containing sequence does not mean that a person having ordinary skill in the art would have any reason or motivation to insert introns into such A/U rich localities, since introns could just as well be inserted into the major part of localities not fulfilling the conditions defined in claim 36. *The Examiner simply fails to provide any reason or motivation for a person having ordinary skill in the art, in view of GenBank Accession No. Z29370 alone or in combination with the other cited references, would know to introduce introns into the A/U rich localities as defined in claim 36.* Consequently, even when the three references, Klimyuk *et al.*, Rose, and GenBank Accession No. Z29370, are simultaneously known to a person having ordinary skill in the art, not all of claim limitations are taught. Instead, it takes the knowledge of the present invention to interpret GenBank Accession No. Z29370 in the sense of Applicants' claimed invention. Accordingly, the

Appl. No.: 10/578,962
Amdt. Dated December 8, 2010
Reply to Office Action of June 8, 2010

Examiner has failed to state a *prima facie* case of obviousness against claims 36-38 based on Klimyuk *et al.* in view of Rose and GenBank Accession No. Z29370.

The Examiner stresses "the teaching of Klimyuk *et al.* that the expression system using viral RNA polymerase is limited by the low ability of RNA polymerase to provide function in trans . . ." (Office Action, p. 5) as a motivation for combining Klimyuk *et al.*, Rose, and GenBank Accession No. Z29370. It is pointed out that the statement made by Klimyuk *et al.* in paragraph [0005] was made in the context of the systems described in U.S. Pat. Nos. 6,093,554 and 5,919,705. U.S. Pat. No. 6,093,554 describes recombinant DNA comprising viral cis-elements for replication, but no gene that codes for the viral RNA/RNA polymerase (see abstract or claim 1 of U.S. Pat. No. 6,093,554). The genetically engineered cross-protection system of U.S. Pat. No. 5,919,706 uses a DNA construct encoding a minus sense RNA molecule capable of interacting with an RNA-dependent RNA polymerase encoded by an invading virus (first paragraph of section "Detailed Description" of U.S. Pat. No. 5,919,705). Thus, the polymerase for the DNA construct in U.S. Pat. No. 5,919,705 is also provided from a different nucleic acid (*i.e.*, the invading virus).

In contrast, the system of Klimyuk *et al.*, as well as the process of the present invention as defined by claim 36, uses RNA replicons that contain sequences for replicon function that code for an RNA-dependent RNA polymerase, whereby the latter is present in *cis*. Thus, the skilled person reading Klimyuk *et al.* understands that the problem referred to in paragraph [0051] of Klimyuk *et al.* has already been overcome by Klimyuk *et al.*, whereby paragraph [0051] of Klimyuk *et al.* cannot provide motivation to a person having ordinary skill in the art for further development of the teaching of Klimyuk *et al.*.

For a person having ordinary skill in the art departing from Klimyuk *et al.*, even the selection of Rose for improving Klimyuk *et al.* requires the knowledge of the present invention, since Klimyuk *et al.* contains no hint to consider Rose, and since a person having ordinary skill in the art wishing to improve Klimyuk *et al.* is confronted with a universe of possibilities without guidance into the direction of the present invention.

Appl. No.: 10/578,962
Amdt. Dated December 8, 2010
Reply to Office Action of June 8, 2010

Moreover, intron-mediated enhancement (referred to as IME) by Rose has been known for a long time. For example, Rose refers on the first page, left column, bottom, to IME and cites a publication from the year 1990. Also, plant viral expression systems wherein cDNA copies of RNA viral vectors are used for plant transformation have been known since the middle of the 1990s. As examples, Applicants submit concurrently hereinwith Turpen *et al.* and Baucombe *et al.* (*see*, Applicants' IDS filed December 8, 2010). Thus, these technologies have co-existed for about 10 years before the priority date of the present patent application. Consequently, if it had been obvious for a person having ordinary skill in the art to combine these technologies as alleged in the Office Action, then the combination should have been made long before the priority date of the present invention. Thus, the fact the combination was not made until the time of Applicants' invention provides further evidence that their claimed invention is not obvious in view of Rose and the other cited references.

For the reasons stated above, Applicants submit that the Examiner has not made a *prima facie* case of obviousness against the amended claims. In view of the above remarks, Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejection of the claims under 35 U.S.C. § 103(a) is overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

Appl. No.: 10/578,962
Amdt. Dated December 8, 2010
Reply to Office Action of June 8, 2010

therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

/david m. saravitz/

David M. Saravitz
Registration No. 55,593

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Research Triangle Area Office (919) 862-2200
Fax Research Triangle Area Office (919) 862-2260

ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON DECEMBER 8, 2010.